

Amendments to the Claims

Claim 1 (currently amended): A nucleic acid polymerase comprising a modification that ~~which has been modified to~~ increases or enhances fidelity, wherein said modification corresponds to amino acid position Arg722, or amino acid position Lys726, or amino acid positions Arg722 and Lys726, or amino acid positions Arg722 and Phe730 of a *Thermotoga neapolitana* ~~neopolitana~~ polymerase, with the proviso that when said modification consists of a single amino acid substitution at either Arg722 or Lys726, said substitution is an amino acid other than Ala, and with the proviso that when said modification consists of an amino acid substitution at Arg722, said substitution is an amino acid other than Pro, Trp, and Gln.

Claim 2 (currently amended): A nucleic acid polymerase comprising a modification that ~~which has been modified to~~ reduces or eliminates misincorporation of nucleotides during nucleic acid synthesis, wherein said modification corresponds to amino acid position Arg722, or amino acid position Lys726, or amino acid positions Arg722 and Lys726, or amino acid positions Arg722 and Phe730 of a *Thermotoga neapolitana* ~~neopolitana~~ polymerase, with the proviso that when said modification consists of a substitution of a single amino acid at either Arg722 or Lys726, said substitution is an amino acid other than Ala, and with the proviso that when said modification consists of an amino acid substitution at Arg722, said substitution is an amino acid other than Pro, Trp, and Gln.

Claim 3 (previously presented): The polymerase of claim 1 or 2, wherein said polymerase is a DNA polymerase.

Claim 4 (previously presented): The polymerase of claim 3, wherein said polymerase is derived from a mesophilic organism or said polymerase is thermostable.

Claim 5 (currently amended): The polymerase of claim 3, wherein said polymerase is derived from a polymerase selected from the group consisting of *The* DNA polymerase, *Taq* DNA polymerase, *Tma* DNA polymerase, *Tth* DNA polymerase, *Tli* (VENTTM) DNA polymerase, *Pfu* DNA polymerase, DEEPVENTTM DNA polymerase, *Pwo* DNA polymerase, *Bst* DNA polymerase, *Bca* DNA polymerase, *Tfl* DNA polymerase, and mutants and fragments thereof.

Claim 6 (previously presented): The polymerase of claim 1 or 2, further comprising one or more modifications to reduce or eliminate one or more activities selected from the group consisting of:

- (a) the 3'→5' exonuclease activity of the polymerase;
- (b) the 5'→3' exonuclease activity of the polymerase; and
- (c) the discriminatory activity against one or more dideoxynucleotides.

Claim 7 (previously presented): The polymerase of claim 1 or claim 2, wherein said polymerase is modified to reduce or eliminate 3'→5' exonuclease activity.

Claim 8 (previously presented): The polymerase of claim 1 or claim 2, wherein said polymerase is modified to reduce or eliminate discriminatory activity against one or more dideoxynucleotides.

Claim 9 (previously presented): The polymerase of claim 1 or claim 2, wherein said polymerase is modified to reduce or eliminate 5'→3' exonuclease activity.

Claim 10 (canceled)

Claim 11 (currently amended) The polymerase of claim 1 or claim 2, wherein said modification is in an O-helix of said polymerase corresponding to
RXXXKXXXFXXXYX (SEQ ID NO:1).

Claim 12 (currently amended): The polymerase of claim 1 or claim 2, wherein said modification corresponds to amino acid position Arg722 ~~R-(Arg722)~~.

Claim 13 (canceled)

Claim 14 (currently amended): The polymerase of claim 12, wherein Arg722 R (~~Arg722~~) is substituted with an amino acid selected from the group consisting of Ala, Asn, Asp, Cys, ~~Gln~~, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, ~~Pro~~, Ser, Thr, ~~Trp~~, Tyr and Val, with the proviso that when said modification consists of a single amino acid substitution, said substitution is not Ala.

Claim 15 (currently amended): The polymerase of claim 1 or claim 2, wherein said modification corresponds to amino acid position Lys726 K (~~Lys726~~).

Claim 16 (canceled)

Claim 17 (currently amended): The polymerase of claim 15, wherein Lys726 K (~~Lys726~~) is substituted with an amino acid selected from the group consisting of Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, with the proviso that when said modification consists of a single amino acid substitution, said substitution is not Ala.

Claim 18 (currently amended): The polymerase of claim 1 or claim 2, wherein said modifications correspond to amino acid at positions Arg722 and Lys726 R (~~Arg722~~) and at position K (~~Lys726~~).

Claim 19 (canceled)

Claim 20 (currently amended): The polymerase of claim 18, wherein Arg722 ~~R~~ (~~Arg722~~) is substituted with an amino acid selected from the group consisting of Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, and wherein Lys726 ~~K~~ (~~Lys726~~) is substituted with an amino acid selected from the group consisting of Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val.

Claims 21-36 (canceled)

Claim 37 (currently amended): A kit for amplifying, synthesizing, or sequencing a DNA molecule comprising one or more of the modified polymerases of claim 1 or claim 2.

Claim 38 (original): The kit of claim 37, further comprising one or more dideoxyribonucleoside triphosphates.

Claim 39 (original): The kit of claim 37, further comprising one or more deoxyribonucleoside triphosphates.

Claim 40 (original): The kit of claim 38, further comprising one or more deoxyribonucleoside triphosphates.

Claims 41-42 (canceled)

Claim 43 (previously presented): The polymerase of claim 1 or 2, wherein said polymerase is a RNA polymerase.

Claim 44 (currently amended): The polymerase of claim 43, wherein said RNA polymerase is derived from a polymerase selected from the group consisting of T3, T5 and SP6.

Claims 45-46 (canceled)

Claim 47 (currently amended): A thermostable nucleic acid polymerase ~~which has been modified, wherein said modification comprising a modification that~~ corresponds to amino acid position Arg722, or amino acid position Lys726, or amino acid positions Arg722 and Lys726, or amino acid positions Arg722 and Phe730 of a *Thermotoga neapolitana* ~~neopolitana~~ polymerase, with the proviso that when said modification consists of a single amino acid substitution at either Arg722 or Lys726, said substitution is an amino acid other than Ala, and with the proviso that when said modification consists of an amino acid substitution at Arg722, said substitution is an amino acid other than Pro, Trp, and Gln.

Claim 48 (previously presented): The polymerase of claim 47, wherein said polymerase is a DNA polymerase.

Claim 49 (canceled)

Claim 50 (currently amended): The polymerase of claim 48, wherein said polymerase is derived from a polymerase selected from the group consisting of *Tne* DNA polymerase, *Taq* DNA polymerase, *Tma* DNA polymerase, *Tth* DNA polymerase, *Tli* (VENTTM) DNA polymerase, *Pfu* DNA polymerase, DEEPVENTTM DNA polymerase, *Pwo* DNA polymerase, *Bst* DNA polymerase, *Bca* DNA polymerase, *Tfl* DNA polymerase, and mutants and fragments thereof.

Claim 51 (previously presented): The polymerase of claim 47, further comprising one or more modifications to reduce or eliminate one or more activities selected from the group consisting of:

- (a) the 3'→5' exonuclease activity of the polymerase;
- (b) the 5'→3' exonuclease activity of the polymerase; and
- (c) the discriminatory activity against one or more dideoxynucleotides.

Claim 52 (previously presented): The polymerase of claim 47, wherein said polymerase is modified to reduce or eliminate 3'→5' exonuclease activity.

Claim 53 (previously presented): The polymerase of claim 47, wherein said polymerase is modified to reduce or eliminate discriminatory activity against one or more dideoxynucleotides.

Claim 54 (previously presented): The polymerase of claim 47, wherein said polymerase is modified to reduce or eliminate 5'→3' exonuclease activity.

Claim 55 (currently amended): The polymerase of claim 47, wherein said modification is in an O-helix of said polymerase corresponding to RXXXKXXXFXXXYX (SEQ ID NO:1).

Claim 56 (currently amended): The polymerase of claim 47, wherein said modification corresponds to amino acid position Arg722 ~~R (Arg722)~~.

Claim 57 (currently amended): The polymerase of claim 56, wherein Arg722 ~~R (Arg722)~~ is substituted with an amino acid selected from the group consisting of Ala, Asn, Asp, Cys, ~~Gln~~, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, ~~Pro~~, Ser, Thr, ~~Trp~~, Tyr and Val, with the proviso that when said modification consists of a single amino acid substitution, said substitution is not Ala.

Claim 58 (currently amended): The polymerase of claim 47, wherein said modification corresponds to amino acid position Lys726 ~~K (Lys726)~~.

Claim 59 (currently amended): The polymerase of claim 58, wherein Lys726 ~~K (Lys726)~~ is substituted with an amino acid selected from the group consisting of Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Pro, Ser, Thr, Trp, Tyr and

Val, with the proviso that when said modification consists of a single amino acid substitution, said substitution is not Ala.

Claim 60 (currently amended): The polymerase of claim 47, wherein said modifications correspond to amino acid at positions Arg722 and Lys726 ~~R (Arg722) and at position K (Lys726)~~.

Claim 61 (currently amended): The polymerase of claim 60, wherein Arg722 ~~R (Arg722)~~ is substituted with an amino acid selected from the group consisting of Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, and wherein Lys726 ~~K (Lys726)~~ is substituted with an amino acid selected from the group consisting of Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val.

Claim 62 (previously presented): The polymerase of claim 47, wherein said polymerase is a RNA polymerase.

Claim 63 (currently amended): The polymerase of claim 62, wherein said RNA polymerase is derived from a polymerase selected from the group consisting of T3, T5 and SP6.

Claim 64 (previously presented): The polymerase of claim 47, wherein said polymerase has substantially reduced or lacks 3'→5' exonuclease activity.

Claim 65 (new): A kit for amplifying, synthesizing, or sequencing a DNA molecule comprising one or more of the modified polymerases of claim 47.

Claim 66 (new): The kit of claim 65, further comprising one or more dideoxyribonucleoside triphosphates.

Claim 67 (new): The kit of claim 65, further comprising one or more deoxyribonucleoside triphosphates.

Claim 68 (new): The kit of claim 66, further comprising one or more deoxyribonucleoside triphosphates.

Claim 69 (new): The polymerase of claim 14, wherein Arg722 is substituted with an amino acid selected from the group consisting of Lys, His, Asn, Tyr, and Leu.

Claim 70 (new): The polymerase of claim 1 or claim 2, wherein said modification corresponds to amino acid positions Arg722 and Phe730.

Claim 71 (new): The polymerase of claim 70, wherein Arg722 is substituted with an amino acid selected from the group consisting of Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, and Phe730 is substituted

with an amino acid selected from the group consisting of Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Pro, Ser, Thr, Trp, Tyr and Val.

Claim 72 (new): The polymerase of claim 71, wherein Arg722 is substituted with an amino acid selected from the group consisting of Lys, Gln, His, Asn, Tyr, and Leu.

Claim 73 (new): The polymerase of claim 71, wherein Phe730 is substituted with Tyr.

Claim 74 (new): The polymerase of claim 71, wherein Arg722 is substituted with an amino acid selected from the group consisting of Lys, Gln, His, Asn, Tyr, and Leu, and Phe730 is substituted with Tyr.

Claim 75 (new): The polymerase of claim 17, wherein Lys726 is substituted with Arg.

Claim 76 (new): The polymerase of claim 57, wherein Arg722 is substituted with an amino acid selected from the group consisting of Lys, His, Asn, Tyr, and Leu.

Claim 77 (new): The polymerase of claim 47, wherein said modification corresponds to amino acid positions Arg722 and Phe730.

Claim 78 (new): The polymerase of claim 76, wherein Arg722 is substituted with an amino acid selected from the group consisting of Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val, and Phe730 is substituted with an amino acid selected from the group consisting of Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Pro, Ser, Thr, Trp, Tyr and Val.

Claim 79 (new): The polymerase of claim 76, wherein Arg722 is substituted with an amino acid selected from the group consisting of Lys, Gln, His, Asn, Tyr, and Leu.

Claim 80 (new): The polymerase of claim 78, wherein Phe730 is substituted with Tyr and.

Claim 81 (new): The polymerase of claim 78, wherein Arg722 is substituted with an amino acid selected from the group consisting of Lys, Gln, His, Asn, Tyr, and Leu, and Phe730 is substituted with Tyr.

Claim 82 (new): The polymerase of claim 58, wherein Lys726 is substituted with Arg.